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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,229	11/17/2003	Tariq M. Rana	UMY-041	5733

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EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/715,229	RANA, TARIQ M.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *18-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-17, in the reply filed on 09/28/2005 is acknowledged.

Status of the Application

Claims 1-34 are pending. Claims 1-17 are currently under examination. Claims 18-34 are withdrawn as being drawn to a non-elected invention.

Priority

The priority date granted to claims 3-9 is 11/26/2002. Applicant does not receive the benefit of the prior applications 60/426,982, 60/430,517, and 60/458,051 because the prior applications do not provide adequate support for the claims of the instant application.

The prior applications each disclose siRNA but only 60/430,517 disclose allele-specific targeting with siRNA. Further, 60/430,517 disclose in Examples 1-3 siRNA comprising base modifications. However, 60/430,517 does not contemplate siRNA targeted to a mutant allele wherein the antisense strand comprises a sequence comprising one or more modified bases positioned opposite the point mutations. If Applicant believes the prior application provides support then applicant must point, with particularity, to where such support can be found in the specification of the prior application.

Therefore, the priority date granted to claims 3-9 is 11/26/2003, the filing date of the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a siRNA comprising a sense strand and an antisense strand wherein the sense strand comprises a sequence homologous to a region of a mutant allele encoding a gain-of-function mutant protein and wherein the antisense strand comprises a sequence comprising one or more modified bases positioned opposite the point mutations wherein the point mutation is an adenine or thymine and further such that the siRNA directs allele-specific cleavage of a mRNA encoded by the mutant allele.

The specification as filed discloses siRNA compounds targeted to cells expressing reporters GFP and RFP (see Examples 1-3). Further, the specification as filed discloses modified siRNA compounds that inhibit expression of GFP and RFP mRNA (see Example 3).

The specification does not provide adequate written description of a siRNA targeted to a sequence comprising point mutations and that directs allele-specific cleavage of an mRNA encoded by a mutant allele. Therefore, in only disclosing siRNA

compounds that are targeted to a gene encoding GFP and RFP and disclosing siRNA compounds that inhibit expression of GFP and RFP, the specification does not provide information on what siRNA compound directs allele-specific cleavage of a mRNA encoded by the mutant allele.

The specification does not provide specific guidance that would allow the skilled artisan to recognize that Applicant was in possession of the instant invention, commensurate in scope with what is now claimed: a siRNA compound directs allele-specific cleavage of a mRNA encoded by the mutant allele. For example, what siRNA structure or sequence would one skilled in the art know or expect would direct allele-specific cleavage of an mRNA encoded by a mutant allele wherein the point mutation is an adenine or a thymine.

Additionally, there are no examples provided of an siRNA that is targeted to a sequence comprising an adenine or thymine point mutation and directs cleavage of a mRNA encoded by a mutant allele and the specification nor the prior art provide a core structure or motif that would impart the function of directing allele-specific cleavage of a mRNA encoded by a mutant allele. Therefore, one is left to empirically screen for siRNA compounds of the invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

MPEP 2163 states in part, "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.").

Thus, the instantly claimed invention cannot be said to have been adequately described in a way that would convey with reasonable clarity to those skilled in the art that, as of the filling date sought, applicant was in possession of the claimed invention

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 and 7 recite the limitation "wherein the point mutation". There is insufficient antecedent basis for this limitation in the claims because claims 6 and 7 are multiple dependent claims of claim 4 which depends from any one of claims 1-3 and claims 1-2 do not recite point mutations.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4-5 and 10-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Tuschl et al. (WO 02/44321).

The instant claims are drawn to a siRNA comprising at least one modified base wherein the modified base is capable of enhancing single nucleotide discrimination between a first target having 1, 2, 3 or more mutations relative to a second target wherein the siRNA is between about 10-50, 15-45, 20-40 or 18-25 residues in length and further drawn to a therapeutic composition comprising the siRNA and a pharmaceutically acceptable carrier, a host cell comprising said siRNA wherein the host cell is mammalian or human.

Tuschl et al. teach a siRNA 19-25 nucleotides in length (see page 4, lines 1-5) further teach a composition comprising a siRNA and a pharmaceutically acceptable

carrier (see page 9, lines 11-16). Tuschl et al. further teach siRNA comprising at least one modified base wherein the modified base comprises 5-bromouracil or 5-iodouracil (page 5, lines 23-31).

Thus, Tuschl et al. anticipates claims 1-2, 4-5 and 10-17 of the instant application.

Claims 3-5 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Xu et al. (US 2004/0192629).

The instant claim is drawn to a siRNA comprising a sense strand and an antisense strand wherein the sense strand comprises a sequence homologous to a region of a mutant allele encoding a gain-of-function mutant protein and wherein the antisense strand comprises a sequence comprising one or more modified bases positioned opposite the point mutations.

Xu et al. teach a siRNA comprising a sequence homologous to a region of a mutant allele encoding SOD1, a mutant protein involved in ALS disease, wherein the antisense strand comprises a sequence positioned opposite a point mutation (see Figure 1). Xu et al. further teach the siRNA can comprise a modified base at any position (see paragraph 0039).

Thus, Xu et al. anticipates claims 3-5 and 9 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-5, 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu et al. (US 2004/0192629) in view of.

The instant claim is drawn to a siRNA comprising a sense strand and an antisense strand wherein the sense strand comprises a sequence homologous to a region of a mutant allele encoding a gain-of-function mutant protein and wherein the antisense strand comprises a sequence comprising one or more modified bases positioned opposite the point mutations and further wherein the modified base is 2,6-diaminopurine.

Xu et al. teach a siRNA comprising a sequence homologous to a region of a mutant allele encoding SOD1, a mutant protein involved in ALS disease, wherein the antisense strand comprises a sequence positioned opposite a point mutation (see Figure 1). Xu et al. further teach the siRNA can comprise a modified base at any position (see paragraph 0039). Xu et al. does not teach a siRNA comprising a modified base is 2,6-diaminopurine.

Buhr et al. teach an oligonucleotide with a 2,6-diaminopurine modified base. Buhr et al. also teach one of ordinary skill to modify nucleobases in antisense oligonucleotides.

It would have been obvious to one of ordinary skill in the art to incorporate modifications as taught by Buhr et al. into said siRNA compounds.

One would have been motivated to modify said siRNA compounds as taught by Buhr et al. because Buhr et al. teach that such modifications increase an antisense compound's resistance to degradation.

Finally, one would have a reasonable expectation of success given that Buhr et al. teach the stability of the modified oligonucleotide compounds.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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1635